

Application No. 10/033,621
 Amendment dated July 21, 2006
 After Final Office Action of March 21, 2006

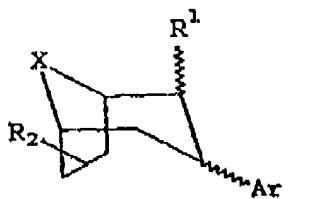
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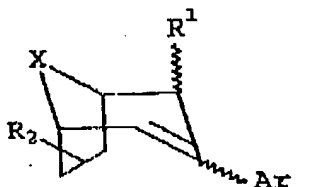
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

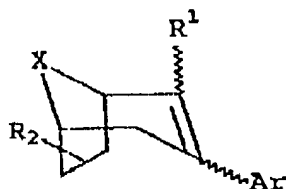
1. (Currently amended) A compound having the structural formula:



or



or



wherein:

$R_1 = \text{COR}_3$, and is α or β ;

$R_2 = \text{OH}$ or O , is a 6- or 7- substituent, and if R_2 is OH , it is α or β ;

$X = \text{NR}_3$ or NSO_2R_3 , with the N being a member of the ring, or $\text{C}=\text{CX}_4\text{Y}$, with the C being a member of the ring;

$X_4 = \text{NR}_4$ or NSO_2R_4 ;

$R_3 = \text{H}$, $(\text{CH}_2)_n\text{C}_6\text{H}_4\text{Y}$, $\text{C}_6\text{H}_4\text{Y}$, CHCH_2 , lower alkyl, lower alkenyl or lower alkynyl;

$\text{Y} = \text{H}$, Br , Cl , I , F , OH , OCH_3 , CF_3 , NO_2 , NH_2 , CN , NHCOCH_3 , $\text{N}(\text{CH}_3)_2$, $(\text{CH}_2)_n\text{CH}_3$,

COCH_3 , or $\text{C}(\text{CH}_3)_3$;

$\text{Ar} = \text{phenyl-}R_5$, $\text{naphthyl-}R_5$, $\text{anthracenyl-}R_5$, $\text{phenanthrenyl-}R_5$, or $\text{diphenylmethoxy-}R_5$;

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$R_5 = \text{H, Br, Cl, I, F, OH, OCH}_3, \text{CF}_3, \text{NO}_2, \text{NH}_2, \text{CN, NHCOCH}_3, \text{N(CH}_3)_2, (\text{CH}_2)_n\text{CH}_3, \text{COCH}_3, \text{C(CH}_3)_3$ where $n = 0-6$, 4-F, 4-Cl, 4-I, 2-F, 2-Cl, 2-I, 3-F, 3-Cl, 3-I, 3,4-diCl, 3,4-diOH, 3,4-diOAc, 3,4-diOCH₃, 3-OH-4-Cl, 3-OH-4-F, 3-Cl-4-OH, 3-F-4-OH, lower alkyl, lower alkoxy, lower alkenyl, lower alkynyl, CO(lower alkyl), or CO(lower alkoxy); and
 $n = 0, 1, 2, 3, 4$ or 5.

2. (Original) The compound of claim 1, which is a 1-S enantiomer.
3. (Original) The compound of claim 1, wherein Ar is a 3 α - group.
4. (Original) The compound of claim 1, wherein Ar is a 3 β - group.
5. (Previously presented) The compound of claim 1, wherein R₂ is OH, and X is NR₃.
6. (Previously presented) The compound of claim 1, wherein the compound has an IC₅₀ SERT/DAT ratio of greater than about 10, preferably greater than about 30 and more preferably 50 or more.
7. (Original) The compound of claim 1, having an IC₅₀ at the DAT of less than about 500 nM, preferably less than 60 nM, more preferably less than about 20, and most preferably less than about 10.
8. (Cancelled)
9. (Previously presented) The compound of claim 1, wherein X is NR₃ or NSO₂R₃, and Ar is phenyl, substituted phenyl, diarylmethoxy or substituted diarylmethoxy.
10. (Original) The compound of claim 9, wherein the substituent is a halogen.
11. (Original) The compound of claim 9, wherein Ar is a mono- or di-halogen substituted phenyl.

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12. (Previously presented) The compound of claim 1, wherein the aryl ring is substituted with one or more halide atoms, hydroxy groups, nitro groups, amino groups, cyano groups, lower alkyl groups having from 1-8 carbon atoms, lower alkoxy groups having from 1-8 carbon atoms, lower alkenyl groups having from 2-8 carbon atoms, or lower alkynyl groups having from 2-8 carbon atoms.

13. (Original) The compound of claim 12, wherein the aryl ring can be substituted with chloride, fluoride or iodide.

14. (Previously presented) The compound of claim 12, wherein an amino group is a mono- or di- alkyl substituted group having from 1-8 carbon atoms.

15. (Original) The compound of claim 12, wherein the aryl group has a substituent selected from the group consisting of Br, Cl, I, F, OH, OCH₃, CF₃, NO₂, NH₂, CN, NHCOCH₃, N(CH₃)₂, COCH₃, C(CH₃)₃, (CH₂)_nCH₃ where n= 0-6, allyl, isopropyl and isobutyl.

16. (Previously presented) The compound of claim 1, wherein the aryl group has a substituent selected from the group consisting of lower alkyl, lower alkenyl and lower alkynyl.

17. (Previously presented) The compound of claim 1, wherein the aryl group is substituted with a member selected from the group consisting of 4-F, 4-Cl, 4-I, 2-F, 2-Cl, 2-I, 3-F, 3-Cl, 3-I, 3,4-diCl, 3,4-diOH, 3,4-diOAc, 3,4-diOCH₃, 3-OH-4-Cl, 3-OH-4-F, 3-Cl-4-OH and 3-F-4-OH.

18. (Original) The compound of claim 9, wherein R₂ is OH.

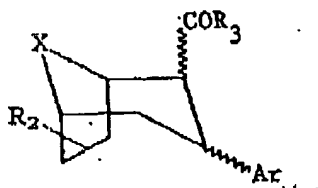
19. (Cancelled)

20. (Previously presented) The compound of claim 1 having the following structural formula:

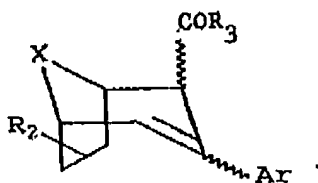
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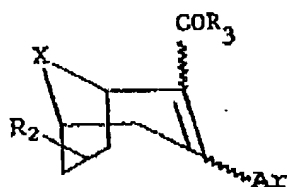
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or



or



where X is NR₃, R₃ is CH₂CH₃, R₂ is OH or O in the 6- or 7- position, Ar is phenyl or naphthyl either of which can be substituted with halogen, alkenyl having 2-8 carbon atoms or alkynyl having 2-8 carbon atoms.

21. (Original) The compound of claim 20, wherein Ar is substituted with 4-Cl, 4-F, 4-Br, 4-I, 3,4-Cl₂, ethenyl, propenyl, butenyl, propynyl or butynyl.

22. (Original) The compound of claim 20, wherein R₂ is OH.

23. (Original) The compound of claim 20 selected from the group consisting of:

a. 1-[3 α -(3,4-Dichlorophenyl)-7 β -hydroxy-8-methyl-8-azabicyclo[3.2.1]oct-2-yl]propan-1-one.

b. 1-[3 β -(3,4-Dichlorophenyl)-7 β -hydroxy-8-methyl-8-azabicyclo[3.2.1]oct-2-yl]propan-1-one.

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24. (Previously presented) The compound of claim 1 selected from the group consisting of:

a. 1-[3 α -(3,4-Dichlorophenyl)-7 β -hydroxy-8-methyl-8-azabicyclo[3.2.1]oct-2-yl]propan-1-one;

b. 1-[3 β -(3,4-Dichlorophenyl)-7 β -hydroxy-8-methyl-8-azabicyclo[3.2.1]oct-2-yl]propan-1-one.

25. - 28. (Cancelled)

29. (Original) A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 1 and a pharmaceutically acceptable carrier.

30. (Previously presented) A method for treating a mammal having a disorder selected from neurodegenerative disease, psychiatric dysfunction, dopamine dysfunction, and cocaine abuse comprising administering to the mammal an effective amount of a compound of claim 1, wherein the Ar is a 3 α -group.

31. (Previously presented) A method for treating a mammal having a disorder selected from neurodegenerative disease, psychiatric dysfunction, dopamine dysfunction, and cocaine abuse comprising administering to the mammal an effective amount of a compound of claim 1.

32. (Cancelled)

33. (Original) A method for treating a neurodegenerative disease in a mammal comprising administering to the mammal an effective amount of a compound of claim 1.

34. (Original) The method of claim 33, wherein the neurodegenerative disease is selected from Parkinson's disease and Alzheimer's disease.

35. (Original) A method for treating psychiatric dysfunction in a mammal comprising administering to the mammal an effective amount of a compound of claim 1.

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36. (Cancelled)

37. (Original) The method according to claim 35, wherein the psychiatric disorder comprises depression.

38. (Cancelled)

39. (Original) A method for treating dopamine related dysfunction in a mammal comprising administering to the mammal a dopamine reuptake inhibiting amount of a compound of claim 1.

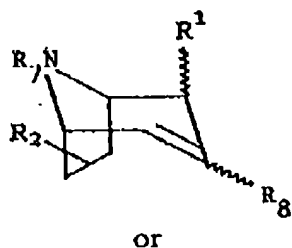
40. (Original) The method according to claim 39, wherein the dopamine related dysfunction comprises Attention deficit disorder.

41. (Original) A method for treating cocaine abuse in a mammal comprising administering to the mammal an effective amount of a compound of claim 1.

42. (Cancelled)

43. (Cancelled)

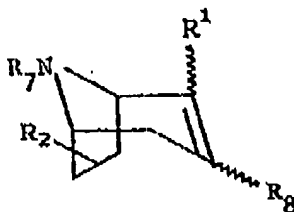
44. (Previously presented) A compound having the structural formula:



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wherein:

$R_1 = \text{COR}_3$, or $\text{CON}(\text{R}_7)\text{OR}_7$ and is α or β ;

$R_2 = \text{OR}_6$ and is a 6- or 7- substituent;

$R_3 = \text{H}$, $(\text{CH}_2)_n\text{C}_6\text{H}_4\text{Y}$, $\text{C}_6\text{H}_4\text{Y}$, CHCH_2 , lower alkyl, lower alkenyl or lower alkynyl;

$\text{Y} = \text{H}$, Br , Cl , I , F , OH , OCH_3 , CF_3 , NO_2 , NH_2 , CN , NHCOCH_3 , $\text{N}(\text{CH}_3)_2$, $(\text{CH}_2)_n\text{CH}_3$,

COCH_3 , or $\text{C}(\text{CH}_3)_3$;

$R_6 = \text{camphanyl}$, phenyl-R_5 , naphthyl-R_5 , anthracenyl-R_5 , phenanthrenyl-R_5 , or $\text{diphenylmethoxy-R}_5$;

$R_5 = \text{H}$, Br , Cl , I , F , OH , OCH_3 , CF_3 , NO_2 , NH_2 , CN , NHCOCH_3 , $\text{N}(\text{CH}_3)_2$, $(\text{CH}_2)_n\text{CH}_3$, COCH_3 , $\text{C}(\text{CH}_3)_3$ where $n = 0-6$, 4-F, 4-Cl, 4-I, 2-F, 2-Cl, 2-I, 3-F, 3-Cl, 3-I, 3,4-diCl, 3,4-diOH, 3,4-diOAc, 3,4-diOCH₃, 3-OH-4-Cl, 3-OH-4-F, 3-Cl-4-OH, 3-F-4-OH, lower alkyl, lower alkoxy, lower alkenyl, lower alkynyl, $\text{CO}(\text{lower alkyl})$, or $\text{CO}(\text{lower alkoxy})$;

$n = 0, 1, 2, 3, 4$ or 5 ;

$R_7 = \text{lower alkyl}$; and

$R_9 = \text{a protecting group}$.

45. (Previously presented) The compound of claim 44 selected from the group consisting of:

a) 2 β -Carbo-N-methoxy-N-methylamino-3 α -(3,4-dichlorophenyl)-7 β -methoxymethoxy-8-methyl-8-azabicyclo[3.2.1]octane;

b) 2 β -Carbo-N-methoxy-N-methylamine-3 β -(3,4-dichlorophenyl)-7 β -methoxymethoxy-8-methyl-8-azabicyclo[3.2.1]octane;

c) 1-[3 α -(3,4-Dichlorophenyl)-7 β -methoxymethoxy-8-methyl-8-azabicyclo[3.2.1]oct-2-yl]propan-1-one; and

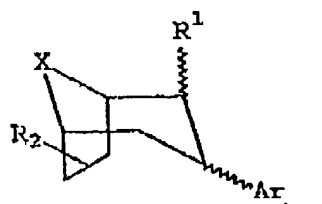
d) 1-[3 β -(3,4-Dichlorophenyl)-7 β -methoxymethoxy-8-methyl-8-azabicyclo[3.2.1]oct-2-yl]propan-1-one.

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46. (Previously presented) A compound having the structural formula:



wherein:

$R_1 = \text{COOR}_7$, COR_3 , lower alkyl, lower alkenyl, lower alkynyl, CONHR_4 , or COR_6 and is

α or β ;

$R_2 = \text{O}$ and is a 6- or 7- substituent;

$X = \text{NR}_3$, with the N being a member of the ring;

$R_3 = \text{H}$, $(\text{CH}_2)_n\text{C}_6\text{H}_4\text{Y}$, $\text{C}_6\text{H}_4\text{Y}$, CHCH_2 , lower alkyl, lower alkenyl or lower alkynyl;

$Y = \text{H}$, Br, Cl, I, F, OH, OCH_3 , CF_3 , NO_2 , NH_2 , CN, NHCOCH_3 , $\text{N}(\text{CH}_3)_2$, $(\text{CH}_2)_n\text{CH}_3$,

COCH_3 , or $\text{C}(\text{CH}_3)_3$;

$R_4 = \text{CH}_3$, CH_2CH_3 , or CH_3SO_2 ;

$R_6 = \text{morpholinyl}$ or piperidinyl ;

$\text{Ar} = \text{phenyl-}R_5$, $\text{naphthyl-}R_5$, $\text{anthracenyl-}R_5$, $\text{phenanthrenyl-}R_5$, or $\text{diphenylmethoxy-}R_5$;

$R_5 = \text{H}$, Br, Cl, I, F, OH, OCH_3 , CF_3 , NO_2 , NH_2 , CN, NHCOCH_3 , $\text{N}(\text{CH}_3)_2$, $(\text{CH}_2)_n\text{CH}_3$,

COCH_3 , $\text{C}(\text{CH}_3)_3$ where $n = 0-6$, 4-F, 4-Cl, 4-I, 2-F, 2-Cl, 2-I, 3-F, 3-Cl, 3-I, 3,4-diCl, 3,4-diOH,

3,4-diOAc, 3,4-diOCH₃, 3-OH-4-Cl, 3-OH-4-F, 3-Cl-4-OH, 3-F-4-OH, lower alkyl, lower alkoxy,

lower alkenyl, lower alkynyl, $\text{CO}(\text{lower alkyl})$, or $\text{CO}(\text{lower alkoxy})$;

$n = 0, 1, 2, 3, 4$ or 5 ; and

$R_7 = \text{lower alkyl}$.

47. (Previously presented) The compound of claim 46, which is a 1-S enantiomer.

48. (Previously presented) The compound of claim 46, wherein Ar is a 3α - group.

49. (Previously presented) The compound of claim 46, wherein Ar is a 3β - group.